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SEARCH REQUEST FORM 58964

Requestor's Name: Natalie Davis Serial Number: 09/819254

Date: 1-25-02 Phone: 308-6410 Art Unit: 1643

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Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search claims 25-32 as they relate to a method of diagnosis or screening for ~~metastatic colorectal cancer~~ stomach cancer by detecting the presence of CDX1 using PCR.

Point of Contact:
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

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Number of Databases: ____

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____ N.A. Sequence
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____ Structure
X Bibliographic

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____ IG Suite
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____ Dialog
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FILE COVERS 1907 - 18 Feb 2002  VOL 136 ISS 8
FILE LAST UPDATED: 17 Feb 2002  (20020217/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d stat que
L7             5 SEA FILE=REGISTRY CDX1/BI
L11              SEL  L7 1- CHEM :      19 TERMS
L12            4 SEA FILE=HCAPLUS L11
L13          694 SEA FILE=HCAPLUS L12 OR CDX1 OR CDXI OR CD(W)XI OR CDX(W)(1 OR
                 I) OR CD11
L14          125 SEA FILE=HCAPLUS L13 (L) (CANCER? OR CARCIN? OR NEOPLASM? OR
                 TUMOR? OR TUMOUR? OR SARCOM? OR LYMPHOM? OR MELANO? OR LEUKEM?
                 OR METAST?)
L16           10 SEA FILE=HCAPLUS L14 AND (PCR OR POLYMERASE (W)CHAIN(W)REACTION
                 ?)


=> d ibib abs hitrn l16 1-10

L16  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:731095  HCAPLUS
DOCUMENT NUMBER:          135:285364
TITLE:                    Compositions and methods for identifying and targeting
                          cancer cells
INVENTOR(S):              Waldman, Scott A.; Park, Jason; Schulz, Stephanie
PATENT ASSIGNEE(S):       Thomas Jefferson University, USA
SOURCE:                   PCT Int. Appl., 119 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
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WO 2001073133	A1	20011004	WO 2001-US9918	20010327
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2001029019	A1	20011011	US 2001-819249	20010327
US 2001029020	A1	20011011	US 2001-819254	20010327
US 2001036635	A1	20011101	US 2001-819247	20010327
US 2001039016	A1	20011108	US 2001-819248	20010327
US 2001039017	A1	20011108	US 2001-819252	20010327
US 2002012931	A1	20020131	US 2001-820215	20010327
PRIORITY APPLN. INFO.:			US 2000-192229 P	20000327

AB Screening and diagnostic reagents, kits and methods for metastatic colorectal cancer or primary and/or metastatic stomach or esophageal cancer are disclosed. Compds., compns. and methods of treating patients with metastatic colorectal cancer or stomach or esophageal cancer and for imaging metastatic colorectal cancer or stomach or esophageal tumors in vivo are disclosed. Compns. and methods for delivering active compds. such as drugs, gene therapeutics and antisense compds. to metastatic colorectal cancer or stomach or esophageal cells are disclosed. Vaccines compns. and methods of for treating and preventing metastatic colorectal cancer or primary and/or metastatic stomach or esophageal cancer are disclosed.

L16 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2001:686789 HCAPLUS
DOCUMENT NUMBER:	136:52169
TITLE:	CDX-1 and CDX-2 are expressed in human colonic mucosa and are down-regulated in patients with Hirschsprung's disease associated enterocolitis
AUTHOR(S):	Lui, V. C. H.; Li, L.; Sham, M. H.; Tam, P. K. H.
CORPORATE SOURCE:	Division of Paediatric Surgery, Department of Surgery, University of Hong Kong Medical Centre, Queen Mary Hospital, Pokfulam, Hong Kong SAR, Peop. Rep. China
SOURCE:	Biochimica et Biophysica Acta (2001), 1537(2), 89-100 CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Caudal type homeobox gene-1 and -2 (**CDX-1** and CDX-2), homologs of the Drosophila homeobox gene caudal, encode transcription factors in endoderm derived tissues of the intestine. CDX genes control proliferation and differentiation of intestinal mucosal cells and colon **cancer** cells. Hirschsprung's Disease (HD) or congenital intestinal aganglionosis, a major developmental anomaly of intestine, which causes functional intestinal obstruction, is frequently assocd. with enterocolitis. Etiol. of HD-assocd. enterocolitis (HDEC) remains obscure. Redn. of gut mucosal enteroendocrine cells, and inefficient transfer of

the secretory IgA across the gut mucosal cell were shown to be assocd. with enterocolitis in HD patients suggesting that mucosa may directly involve in the pathophysiol. of HDEC. This study aims to ascertain whether the **CDX-1** and CDX-2 genes, that control the proliferation and differentiation of mucosal cells, play a role in HDEC. Using semi-quant. reverse transcription-**polymerase chain reaction** (RT-**PCR**) and in situ hybridization, the authors analyzed the expression of **CDX-1** and CDX-2 genes in colon specimens of normal controls, necrotizing enterocolitis (NEC) infants, and HD patients with and without enterocolitis. The authors showed for the first time that **CDX-1** and CDX-2 genes were expressed in the colonic mucosal epithelium in normal, NEC and in HD infants. However, the expressions of both genes were reduced in patients with HDEC. The authors' findings suggest that reduced expression of **CDX-1** and CDX-2 genes in mucosa may be assocd. with the development of HDEC.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:601290 HCAPLUS
DOCUMENT NUMBER: 133:279647
TITLE: Distinct expression of CDX2 and GATA4/5, development-related genes, in human gastric cancer cell lines
AUTHOR(S): Bai, Yun-Qing; Akiyama, Yoshimitsu; Nagasaki, Hiromi; Yagi, Osmar Kenji; Kikuchi, Yoko; Saito, Naoya; Takeshita, Kimiya; Iwai, Takehisa; Yuasa, Yasuhito
CORPORATE SOURCE: Department of Surgery, Tokyo Medical and Dental University School of Medicine, Tokyo, 113-8519, Japan
SOURCE: Mol. Carcinog. (2000), 28(3), 184-188 April 2000 - Accepted
CODEN: MOCAE8; ISSN: 0899-1987
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CDX2 is a **tumor**-suppressor homeobox gene involved in colon **carcinogenesis**, but its role in gastric **cancer** is unknown. Although GATA4, -5 and, -6 transcription factors have distinct functions in the regulation of gastrointestinal epithelial cell differentiation, there have been no reports regarding GATA4/5/6 alterations in gastrointestinal **carcinomas**. By using a semiquant. reverse transcription-**polymerase chain reaction** assay, we studied the expression of gut development-related genes CDX2/1 and GATA4/5/6 in 11 human gastric **cancer** cell lines. The expression of CDX2 appeared to progressively decrease with the transition from well differentiated to poorly differentiated **cancer** cell lines. **CDX1** was below detectable levels in all cell lines. The expression of GATA4 and GATA5 was undetectable in four and six cell lines, resp., whereas the majority of the cell lines expressed GATA6 abundantly. These results suggest that CDX2 and GATA4/5 may be assocd. with the **carcinogenesis** of the stomach.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:369402 HCAPLUS
DOCUMENT NUMBER: 133:148417
TITLE: Deregulated expression of homeobox-containing genes, HOXB6, B8, C8, C9, and **Cdx-1**, in human colon **cancer** cell lines
AUTHOR(S): Vider, Ben-Zion; Zimber, Amazia; Chastre, Eric; Gespach, Christian; Halperin, Marisa; Mashiah, Pnina; Yaniv, Abraham; Gazit, Arnona
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv-Jaffa, 69978, Israel
SOURCE: Biochem. Biophys. Res. Commun. (2000), 272(2), 513-518
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previously we have demonstrated a reciprocal deregulation of various homeobox genes (HOXB6, B8, C8 and C9 vs **Cdx-1**) in human colorectal **cancer** (CRC). In the present study, using RT-**PCR**, we have investigated the expression pattern of these homeobox genes in various human colon cell lines, representing various stages of colon **cancer** progression and differentiation. Thus, we have tested polyposis coli Pc/AA adenoma cells, Caco-2, HT-29 and LS174T adenocarcinoma cell lines. All cell lines, except LS174T, demonstrated a pattern of deregulated homeobox gene expression which resembled that of CRC. In contrast, the pattern of expression of these genes in the highly oncogenic LS174T cells, as well as in Caco-2 cells transfected with activated Ha-ras or Polyoma middle T oncogene, resembled that of the normal mucosa. The reciprocal deregulation of HOX and **Cdx-1** genes in CRC and in CRC-derived cell lines suggests a possible role in human CRC development. (c) 2000 Academic Press.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:605451 HCAPLUS
DOCUMENT NUMBER: 132:206804
TITLE: An immunophenotypic study of canine leukemias and preliminary assessment of clonality by **polymerase chain reaction**
AUTHOR(S): Vernau, W.; Moore, P. F.
CORPORATE SOURCE: School of Veterinary Medicine, Microbiology and Immunology, Department of Pathology, University of California, Davis, CA, USA
SOURCE: Vet. Immunol. Immunopathol. (1999), 69(2-4), 145-164
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is a relative lack of information in the veterinary literature regarding the immunophenotypes present in canine leukemias. Utilizing a panel of thirty monoclonal antibodies, canine leukemias were assessed by

flow cytometry alone or by flow cytometry in combination with immunocytochem. staining of smears. Canine chronic lymphocytic leukemia (CLL) occurred in older dogs (mean age 9.75 yr; range 1.5-15 yr; cases). Blood lymphocyte counts ranged from 15,000 to 1,600,000/.mu.l. Surprisingly, 73% of CLL cases involved proliferation of T lymphocytes (CD3+), and 54% of CLL cases had large granular lymphocyte (LGL) morphol. LGL CLL's were almost exclusively proliferation's of T cells that expressed CD8 and the leukointegrin .alpha.D.beta.2 and more frequently expressed T cell receptor (TCR) .alpha..beta. (69%) than TCR.gamma..delta. (31%). The non-LGL T cell CLL cases (19% of CLL) involved proliferation of TCR.alpha..beta. T cells in which no consistent pattern of CD4 or CD8 expression was found. B cell CLL, based on expression of CD21 or CD79a, comprised 26% of canine CLL cases. These results are in marked contrast to people where greater than 95% of CLL cases involve proliferation of B lymphocytes. Thirty eight (38) acute leukemias were also immunophenotyped. The majority (55%) of these leukemias had a phenotype most consistent with a myeloid origin. Acute LGL leukemias were also obsd. (7/38), although less commonly than the CLL counterpart. CD34 expression was common in acute, non-LGL leukemias of dogs, both myeloid and lymphoid. In some circumstances, it can be difficult to differentiate a reactive (polyclonal) lymphoid proliferation from a neoplastic (monoclonal) one. Therefore, as an adjunct to phenotypic studies, the authors have developed a **polymerase chain reaction** (**PCR**) based test for assessment of clonality in T cell proliferations. The test amplifies the junction of the variable .gamma. (V.gamma.) and joining .gamma. (J.gamma.) gene segments region of the TCR .gamma. genes. Preliminary data indicates that the test is effective and is capable of differentiating a neoplastic from a reactive lymphoproliferative process.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:260372 HCAPLUS
DOCUMENT NUMBER: 126:328868
TITLE: Human colorectal carcinogenesis is associated with deregulation of homeobox gene expression
AUTHOR(S): Vider, Ben Zion; Zimber, Amazia; Hirsch, Dania; Estlein, Dov; Chastre, Eric; Prevot, Sophie; Gespach, Christian; Yaniv, Abraham; Gazit, Arnona
CORPORATE SOURCE: Dep. Human Microbiology, Tel Aviv Univ., Tel Aviv-Jaffa, 69978, Israel
SOURCE: Biochem. Biophys. Res. Commun. (1997), 232(3), 742-748
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the possible involvement of homeobox-contg. genes in colorectal **cancer** (CRC) development was investigated. Using a stepwise screening approach and RT-**PCR**, the authors have demonstrated that the human HOXB6, B8, C8 and C9 are overexpressed at various stages of CRC. In contrast, all CRC cases exhibited a marked decrease in the homeodomain-contg. **Cdx1** gene expression. Recent data which suggest a regulatory link between HOXB8 and several

tumor suppressor genes, such as DCC, APC, and TGF.beta., sustain a possible implication of homeobox genes in colon **carcinogenesis**. Moreover, the authors' data showing a decrease in **Cdx1** expression are consistent with the notion that genes functioning in the establishment and maintenance of the intestinal epithelium might, upon deregulation, disturb the normal control of cellular proliferation, differentiation, and death, thus leading to **cancer** development.

L16 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:194390 HCAPLUS
DOCUMENT NUMBER: 126:208069
TITLE: Molecular cloning, sequencing and expression of the mRNA encoding human **Cdx1** and Cdx2 homeobox. Down-regulation of **Cdx1** and Cdx2 mRNA expression during colorectal **carcinogenesis**
AUTHOR(S): Mallo, Gustavo V.; Rechreche, Hocine; Frigerio, Jean-Marc; Rocha, Dominique; Zweibaum, Alain; Lacasa, Michel; Jordan, Bertrand R.; Dusetti, Nelson J.; Dagorn, Jean-Charles; Iovanna, Juan L.
CORPORATE SOURCE: U.315 INSERM, Marseille, F-13009, Fr.
SOURCE: Int. J. Cancer (1997), 74(1), 35-44
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Defining the mol. mechanisms involved in **cancer** formation and progression is still a major challenge in colorectal-**cancer** research. Our strategy was to characterize genes whose expression is altered during colorectal **carcinogenesis**. To this end, the phenotype of a colorectal **tumor** was previously established by partial sequencing of a large no. of its transcripts and the genes of interest were selected by differential screening on high-d. filters with mRNA of colorectal **cancer** and normal adjacent mucosa. Fifty-one clones were found over-expressed, and 23 were under-expressed in the colorectal-**cancer** tissues of the 5 analyzed patients. Among the latter, clones 6G2 and 32D6 were found of particular interest, since they had significant homol. with several homeodomain-contg. genes. The highest degree of similarity was with the murine **Cdx1** for 6G2, and with the murine Cdx2 and hamster Cdx3 for 32D6. Using a RT-**PCR** approach, complete sequence of both types of homeobox-contg. cDNA was obtained. The amino-acid sequence of the human **Cdx1** is 85% identical to the mouse protein, and human Cdx2 has 94% identity with the mouse Cdx2 and hamster Cdx3. Tissue-distribution anal. of **Cdx1** and Cdx2 mRNA showed that both transcripts were specifically expressed in small intestine, in colon and rectum. Twelve tissue samples from colorectal adenocarcinomas and the corresponding normal mucosa were analyzed by Northern blot. Expression of the 2 types of mRNA was either reduced or absent in 10 of them. Several colon-**cancer** cell lines were also analyzed. Cdx2 mRNA was absent from LS174T cells and **Cdx1** mRNA was absent in PF11, TC7 and SW480 cells; none was detected in HT29 cells. It was concluded that decrease in human **Cdx1** and/or Cdx2 expression is assocd. with colorectal **tumorigenesis**.

IT **170560-45-9**

RL: PRP (Properties)
(amino acid sequence; mol. cloning, sequencing and expression of the mRNA encoding human **Cdx1** and Cdx2 homeobox. Down-regulation of **Cdx1** and Cdx2 mRNA expression during colorectal **carcinogenesis**)

IT **185238-80-6, Genbank U51095**
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(nucleotide sequence; mol. cloning, sequencing and expression of the mRNA encoding human **Cdx1** and Cdx2 homeobox. Down-regulation of **Cdx1** and Cdx2 mRNA expression during colorectal **carcinogenesis**)

L16 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:151554 HCAPLUS
DOCUMENT NUMBER: 124:228310
TITLE: Human melanoma integrins contribute to arrest and stabilization potential while flowing over extracellular matrix
AUTHOR(S): Menter, David G; Fitzgerald, Larry; Patton, John T; Mcintire, Larry V; Nicolson, Garth L
CORPORATE SOURCE: MD Anderson Cancer Center, University of Texas, Houston, TX, 77251, USA
SOURCE: Immunol. Cell Biol. (1995), Volume Date 1995, 73(6), 575-83
CODEN: ICBIEZ; ISSN: 0818-9641
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To form distant **metastases**, **tumor** cells must stabilize adhesive interactions that prevent detachment at secondary sites. Primary receptor-ligand interactions alone may not maintain prolonged adhesive contacts without secondary events that lead to adhesion stabilization. Computerized imaging methods enable the authors' to examine various substrates for: (i) the wall shear adhesion threshold (WSAT), a measure of the dynamic adhesive potential of **tumor** cells; (ii) the no. of **tumor** cells that adhered; and (iii) the adhesion stabilization lag time (ASLT) or length of time required for **tumor** cells to stabilize adhesive contacts capable of withstanding high wall shear force (up to 100 dynes/cm2). The relative WSAT ratios found were: wheat germ agglutinin (WGA) > laminin > fibronectin > vitronectin > collagen I > collagen IV > von Willebrand factor (vWF) (the greater the shear rate the higher the adhesive potential). The relative stabilization ratios found were as follows: laminin < fibronectin < vitronectin < collagen IV < collagen I < vWF < WGA (shorter times correlate with greater stabilization potential). Stabilization data using fibronectin as a substrate correlated the best with **metastatic** potential. Using three **melanoma** lines of different **metastatic** potential semiquant. reverse transcriptase-**polymerase chain reaction** (**PCR**) showed a two- to four-fold increase in .alpha.1, .alpha.3, .alpha.4, .alpha.5, .alpha.6, and ICAM-1 in the highly **metastatic** 70W cells compared to the MeWo and non-**metastatic** 3S5 **melanoma** cells. There were no differences in .alpha.v, .beta.1 and .beta.3 levels among the three **melanoma** lines, and **PCR** products for .alpha.IIb,

.alpha.2, CD36, or ICAM-2 were not detected. The 70W cells also had higher levels of .alpha.x and .beta.2 (**CD11**/CD18 and p150 leukocyte antigen) than either the MeWo or 3S5 cells. The data indicate that **melanoma** cells exhibit differences in the adhesion properties under fluid shear and differences in the expression of adhesion components that correlate with their **metastatic** potential.

L16 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:800277 HCAPLUS
DOCUMENT NUMBER: 123:307449
TITLE: Improved transfer of the leukocyte integrin CD18 subunit into hematopoietic cell lines by using retroviral vectors having a gibbon ape leukemia virus envelope
AUTHOR(S): Bauer, Thomas R., Jr.; Miller, A. Dusty; Hickstein, Dennis D.
CORPORATE SOURCE: Medical Res. Service, Seattle VA Medical Center, Seattle, WA, USA
SOURCE: Blood (1995), 86(6), 2379-87
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Leukocyte adherence deficiency (LAD) is an inherited immunodeficiency disease caused by defects in the CD18 leukocyte integrin subunit. Transduction of CD18 into hematopoietic cells from children with LAD represents a potential therapy for this disorder. To maximize transfer and expression of CD18, the authors evaluated retroviral vectors with and without the neomycin selectable marker, with a modified tRNA primer-binding site designed to prevent inhibition of gene expression, and with 2 different viral envelope proteins produced by using the amphotropic retrovirus packaging cell line PA317 or the gibbon ape **leukemia** virus packaging cell line PA317 or the gibbon ape **leukemia** virus packaging cell line PG13. The vectors were tested using transducing K562/CD11b cells and LAD Epstein-Barr virus (EBV) B cells and measuring levels of cell-surface **CD11**/CD18 expression by fluorescence-activated cell sorter anal. The best results were obtained with vectors made using PG13 packaging cells, for which .apprx.25% of the K562 cells exposed once to the vectors expressed surface CD11b/CD18 and about 25% of the LAD EBV B cells exposed 3 times over a 3-day period to the vectors expressed surface CD11a/CD18. In contrast, transduction of cells under similar conditions with retroviral vectors produced using PA317 producer cells yielded <2% .omega.f the KZ462 cells and <4% of the LAD EBV B cells expressing the **CD11**/CD18 heterodimer on the cell surface. The presence or absence of the neomycin resistance gene or the modified tRNA primer had no effect on CD18 gene transfer rate or expression level. The increase in transduction with PG13 vectors correlated with Northern blotting and reverse transcription-**polymerase chain reaction** studies that indicated that both K562 cells and the LAD EBV B cells express transcripts for the gibbon ape **leukemia** virus receptor at higher levels than for the amphotropic virus receptor. Thus, the transduction efficiency of retroviral packaging cell lines correlates with receptor gene expression in the target cells, and vectors made using PGT3 cells may be efficacious for gene therapy for LAD and other diseases in which gene transfer to

hematopoietic cells is required.

L16 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:533636 HCAPLUS
DOCUMENT NUMBER: 115:133636
TITLE: A monoclonal antibody to the human leukocyte adhesion molecule intercellular adhesion molecule-2. Cellular distribution and molecular characterization of the antigen
AUTHOR(S): Nortamo, Pekka; Salcedo, Rosalba; Timonen, Tuomo; Patarroyo, Manuel; Gahmberg, Carl G.
CORPORATE SOURCE: Dep. Biochem., Univ. Helsinki, Helsinki, Finland
SOURCE: J. Immunol. (1991), 146(8), 2530-5
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The DNA of the human leukocyte adhesion mol. intercellular adhesion mol.-2 (ICAM-2) was synthesized by the **polymerase chain reaction**, and a protein A-ICAM-2 fusion protein was expressed in Escherichia coli. The fusion protein was used as immunogen to obtain mAb to ICAM-2. The 6D5 antibody was selected by its reactivity in immunofluorescence with the endothelial cell line Eahy926. The antibody pptd. a 55,000 mol. wt. glycoprotein from radioactively surface labeled cells and also reacted in Western blotting. As measured by immunofluorescence flow cytometry, the antibody reacted with lymphoblastoid B cells of normal origin, some Burkitt **lymphoma** cell lines, vascular endothelial cells, the endothelial cell line Eahy926, and a subpopulation of Con A-stimulated blood mononuclear cells. The two Ig-like domains of ICAM-2 were sep. expressed in E. coli, and the antibody was shown to react with the N-terminal domain. The antibody inhibited the **CD11**/CD18-dependent binding of HL-60 promyelocytic **leukemia** cells to transfected COS-1 cells.

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L7            5 SEA FILE=REGISTRY CDX1/BI
L11             SEL  L7 1- CHEM :      19 TERMS
L12           4 SEA FILE=HCAPLUS L11
L13         694 SEA FILE=HCAPLUS L12 OR CDX1 OR CDXI OR CD(W)XI OR CDX(W)(1 OR
                I) OR CD11
L14         125 SEA FILE=HCAPLUS L13 (L) (CANCER? OR CARCIN? OR NEOPLASM? OR
                TUMOR? OR TUMOUR? OR SARCOM? OR LYMPHOM? OR MELANO? OR LEUKEM?
                OR METAST?)
L15          46 SEA FILE=HCAPLUS L14 AND (PCR OR POLYMERASE (W)CHAIN(W)REACTION
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                DETECT? OR DETN OR DETERMIN? OR IDENT?)
L16          10 SEA FILE=HCAPLUS L14 AND (PCR OR POLYMERASE (W)CHAIN(W)REACTION
                ?)
L17          36 SEA FILE=HCAPLUS L15 NOT L16

=> d ibib abs hitrn l17 1-36

L17 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2002 ACS
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ACCESSION NUMBER: 2002:59305 HCAPLUS
TITLE: The Caudal-related homeodomain protein **CDX1** activates proliferating cell nuclear antigen expression in hepatocellular and colorectal **carcinoma** cells
AUTHOR(S): Oh, Eun-Jin; Park, Jae-Hong; Cho, Mong; Lee, Won-Jae; Choi, Yung Hyun; Yoo, Mi-Ae
CORPORATE SOURCE: Department of Molecular Biology, Pusan National University, Pusan, 609-735, S. Korea
SOURCE: International Journal of Oncology (2002), 20(1), 23-29
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Cdx1** and Cdx2 are known as Caudal-related homeodomain transcription factors important in the early differentiation and maintenance of intestinal epithelial cells. **Cdx1** and Cdx2 are expressed in the small intestine and colon of fetus and adult. Most previous studies suggested that Cdx2 inhibits proliferation. Several target genes of Cdx2 have been **identified**. However, the effect of **Cdx1** on cell proliferation is currently controversial and its target genes except for Hox-A7 remain unknown. In this study, we found several potential Caudal-related homeodomain binding sequences in the 5-flanking region of human PCNA gene. Cotransfection expts., using human PCNA reporter plasmid and **CDX1** and CDX2 expression plasmids, showed that **CDX1** transactivates human PCNA gene promoter activity in hepatocellular cell line (HepG2) and colorectal **carcinoma** cell lines (Colo320HSR and HCT116), while CDX2 does not. **CDX1**-induced PCNA expression was also **detected** in immunoblot and cytochem. expts. In BrdU incorporation expts., **CDX1** enhanced the incorporated BrdU. Taken together, our results suggest that **CDX1** have a pro-proliferative effect on proliferation through transactivation of PCNA promoter activity.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:41281 HCAPLUS
TITLE: Ectopic expression of homeodomain protein CDX2 in intestinal metaplasia and carcinomas of the stomach
AUTHOR(S): Bai, Yun-Qing; Yamamoto, Hiroshi; Akiyama, Yoshimitsu; Tanaka, Hiroyuki; Takizawa, Touichirou; Koike, Morio; Kenji Yagi, Osmar; Saitoh, Kiyoshi; Takeshita, Kimiya; Iwai, Takehisa; Yuasa, Yasuhito
CORPORATE SOURCE: Department of Surgery, Tokyo Medical and Dental University, Graduate School of Medicine and Dentistry, Tokyo, Japan
SOURCE: Cancer Letters (Shannon, Ireland) (2002), 176(1), 47-55
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The roles of CDX2 and **CDX1** homeobox genes during gastric

carcinogenesis remain poorly defined. We have studied the expression of CDX2/1 in gastric **cancers** and intestinal metaplasia (IM) of 69 gastric **carcinoma** patients by immunohistochem. CDX2/1 were shown to be ectopically overexpressed in IM in 41 (85%) of 48, and 47 (90%) of 52 cases, resp. The expression of CDX2/1 was **detected** in 38 (55%) and 51 (74%) of the 69 gastric **carcinomas**, resp. The histol. type of the gastric **carcinomas** was independently assocd. with CDX2 expression, but not with that of **CDX1**, with higher CDX2 expression in intestinal type (differentiated type) than in diffuse type (undifferentiated type) gastric **carcinomas**. Our results thus suggest that CDX2 and **CDX1** may play a role during IM formation and gastric **carcinogenesis**.

L17 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:920784 HCAPLUS
TITLE: The leukocyte integrins are regulated by transcriptional and post-transcriptional mechanisms in a leukemic cell that overexpresses protein kinase C-.xi.
AUTHOR(S): Noti, John D.; Reinemann, Bruce C.; Johnson, Andrew K.
CORPORATE SOURCE: Laboratory of Molecular Biology, Guthrie Research Institute, Sayre, PA, 18840, USA
SOURCE: International Journal of Oncology (2001), 19(6), 1311-1318
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Overexpression of protein kinase C-.xi. (PKC-.xi.) in the **leukemic** myeloid cell line U937 (U937-PKC-.xi. cells), previously shown to induce **leukemic** cell differentiation, resulted in nearly complete downregulation of leukocyte integrins CD11a, CD11b, CD11d, and CD18, but not CD11c from the cell surface. The steady-state level of mRNAs for the downregulated leukocyte integrins was not **detectable** by Northern anal. Nuclear run-on anal. revealed that transcription of all the leukocyte integrin genes except CD11c was reduced 70-90% as compared to control U937-Vector cells [U937 cells transfected with the empty vector pSV2M(2)6]. Transfection anal. of **CD11**-promoter-luciferase constructs confirmed that transcription of the leukocyte integrin genes was drastically downregulated in U937-PKC-.xi. cells. The two c-jun binding sites in the CD11c promoter were essential for continued expression of CD11c in U937-PKC-.xi. cells. Addnl., the 3' untranslated region (3' UTR) from CD11b, when fused to the luciferase gene, lead to the destabilization of this chimeric mRNA in U937-PKC-.xi. cells. This indicates that downregulation of CD11b expression in U937-PKC-.xi. cells is also the result of reduced stability of CD11b mRNA. Thus, overexpression of PKC-.xi. in U937 cells leads not only to **leukemic** cell differentiation, but also to differential regulation of the leukocyte integrins.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:695074 HCAPLUS
DOCUMENT NUMBER: 135:370360
TITLE: A proteolytically truncated form of free CD18, the common chain of leukocyte integrins, as a novel marker of activated myeloid cells
AUTHOR(S): Drbal, Karel; Angelisova, Pavla; Hilgert, Ivan; Cerny, Jan; Novak, Petr; Horejsi, Vaclav
CORPORATE SOURCE: Institute of Molecular Genetics and Institute of Microbiology, Academy of Sciences of the Czech Republic and Faculty of Sciences, Charles University, Prague, Czech Rep.
SOURCE: Blood (2001), 98(5), 1561-1566
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An unusual CD18 monoclonal antibody (mAb) MEM-148 binds, in contrast to std. CD18 mAbs, specifically to peripheral blood monocytes and neutrophils activated by various stimuli such as phorbol myristate acetate, opsonized zymosan, heat-aggregated Ig, and (after priming with lipopolysaccharide, **tumor** necrosis factor, or granulocyte-macrophage colony-stimulating factor) also by formyl-methionyl-leucyl-phenylalanine. In addn., in vivo activated neutrophils obtained from urine of patients following recent prostatectomy were also strongly pos. for MEM-148. On the activated myeloid cells the mAb recognized a 65- to 70 kDa protein **identified** immunochem. and by mass spectrometric peptide sequencing as a membrane-anchored fragment of CD18 (the common chain of leukocyte integrins) produced by proteolytic cleavage. The CD18 fragment originated mainly from integrin mols. stored intracellularly in resting cells, it was unassocd. with **CD11** chains, and its formation was inhibited by several types of protease inhibitors. Thus, the 65- to 70 kDa CD18 fragment represents a novel abundant activation marker of myeloid cells of so far unknown function but possibly involved in conformational changes in leukocyte integrin mols. resulting in increased affinity to their ligands.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:483750 HCAPLUS
TITLE: Characterization of four cell lines derived from a human malignant fibrous histiocytoma of the maxillary sinus
AUTHOR(S): Mori, A.; Tagawa, T.; Kamei, T.; Murata, T.; Inui, M.; Ohse, S.
CORPORATE SOURCE: Faculty of Medicine, Department of Oral and Maxillofacial Surgery, Mie University, Tsu city, Mie, 514-8507, Japan
SOURCE: Oral Oncol. (2001), 37(6), 527-536
CODEN: EJCCER; ISSN: 1368-8375
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have established four cell lines from a human malignant fibrous

histiocytoma. Each cell line had human aneuploid karyotype and DNA aneuploidy. Cells in all lines expressed CD13, CD68 and vimentin but lacked **CD11**, CD14, CD15, CD16, CD45, HLA class II and other mesenchymal and epithelial markers such as desmin, .alpha.-smooth muscle, myoglobin, S-100 protein, and cytokeratin. None of the cells expressed surface IgG or C3 receptor, nor did any of them phagocytose latex particles. The cells reacted with an antibody for prolyl-4-hydroxylase, but no collagen (types I, II, III, or IV) was **detected** in any of the cell lines. The homogenates of all cell lines had cyclic nucleotide phosphodiesterase 3 activity. Two cell lines produced granulocyte colony-stimulating factor (G-CSF), interleukin (IL)-1.alpha., IL-6 and **tumor** necrosis factor .alpha., another line produced G-CSF, IL-1.alpha., IL-6 and platelet-derived growth factor (PDGF)-AB, and the remaining cell line produced only PDGF-AB. None of the cells produced transforming growth factor-.alpha.. The results indicated that the cell lines were immunophenotypically similar to primitive mesenchymal cells.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:535664 HCAPLUS
DOCUMENT NUMBER: 133:236773
TITLE: Comparative analysis of integrin expression on monocyte-derived macrophages and monocyte-derived dendritic cells
AUTHOR(S): Ammon, C.; Meyer, S. P.; Schwarzfischer, L.; Krause, S. W.; Andreesen, R.; Kreutz, M.
CORPORATE SOURCE: Department of Haematology and Oncology, University of Regensburg, Regensburg, D 93042, Germany
SOURCE: Immunology (2000), 100(3), 364-369
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both macrophages (MAC) and dendritic cells (DC) are members of the mononuclear phagocyte system (MPS) with monocytes (MO) as common precursor cells. Cells of the MPS are able to take up, process and present antigens to T lymphocytes, thereby inducing a primary or secondary immune response. Adhesion mols. are of crucial importance for the interaction of antigen-presenting cells with immune cells, esp. T lymphocytes. By representational difference anal., we **identified** CD49c (VLA-3), a member of the .beta.1-integrin family of adhesion receptors, as differentiation-assocd. antigen in MO-derived MAC. In contrast, MO-derived DC did not express CD49c mRNA. These data prompted the authors to compare the integrin expression pattern of MAC and DC. Both cell types showed a low expression of the .alpha.-chains of the .beta.1-integrins CD49a, CD49b, CD49d and CD49e, whereas a marked difference was obsd. for CD49c and CD49f. Expression of both integrins increased during MO to MAC differentiation, but was not **detectable** on DC. In parallel the .beta.1-chain (CD29) was clearly up-regulated during MO to MAC differentiation but was only weakly expressed on DC. On the other hand, the .beta.2-integrins CD11a, CD11b, CD11c and CD18 were all expressed on MAC and DC. Beside their role in cell-cell interaction and adhesion, .beta.2-integrins are also known as possible binding mols. for bacteria

and lipopolysaccharide (LPS), esp. for high LPS concns. Therefore we investigated the LPS response of MAC vs. DC in terms of **tumor** necrosis factor-.alpha. (TNF-.alpha.) release. DC were less responsive to low doses of LPS, which can easily be explained by the very low CD14 expression on DC compared for MAC. In contrast, the TNF-.alpha. response was comparable to MAC when DC were stimulated with high LPS concns. These results show a specific, differentiation-dependent pattern of .beta.1- and .beta.2-integrin expression on in vitro-generated MAC and DC. The high expression of **CD11**/CD18 on DC could be involved in the LPS binding of DC. As LPS is not only an activation but also a differentiation stimulus for DC, the expression of **CD11**/CD18 on DC may be important for the successful maturation of DC and thereby the initiation of a primary immune response.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:261718 HCAPLUS
DOCUMENT NUMBER: 133:29407
TITLE: Synthetic peptides of CD66a stimulate neutrophil adhesion to endothelial cells
AUTHOR(S): Skubitz, Keith M.; Campbell, Kenneth D.; Skubitz, Amy P. N.
CORPORATE SOURCE: Department of Medicine, University of Minnesota Medical School and the Masonic Cancer Center, Minneapolis, MN, 55455, USA
SOURCE: J. Immunol. (2000), 164(8), 4257-4264
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four members of the **carcinoembryonic** Ag family, CD66a, CD66b, CD66c, and CD66d, are expressed on human neutrophils. CD66a, CD66b, CD66c, and CD66d Ab binding to the neutrophil surface triggers an activation signal that regulates the adhesive activity of **CD11**/CD18, resulting in an increase in neutrophil adhesion to HUVEC. To **identify** active sites on the CD66a Ag, mol. modeling was performed using IgG and CD4 as models, and 28 peptides of 14 aa in length were synthesized that were predicted to be present at loops and turns between .beta.-sheets. The peptides were tested for their ability to alter neutrophil adhesion to HUVEC. Three peptides, each from the N-terminal domain, increased neutrophil adhesion to HUVEC monolayers. This increase in neutrophil adhesion caused by CD66a peptides was assocd. with up-regulation of **CD11**/CD18 and down-regulation of CD62L on the neutrophil surface. Scrambled versions of these three peptides had no effect on neutrophil adhesion to the endothelial cells. The data suggest that peptide motifs from at least three regions of the N-terminal domain of CD66a are involved in the interaction of CD66a with other ligands and can initiate signal transduction in neutrophils.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:399820 HCAPLUS

DOCUMENT NUMBER: 131:168005
TITLE: The Cdx-1 and Cdx-2 homeobox genes in the intestine
AUTHOR(S): Freund, Jean-Noel; Domon-Dell, Claire; Kedinger, Michele; Duluc, Isabelle
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale, Unite 381, Strasbourg, 67200, Fr.
SOURCE: Biochem. Cell Biol. (1998), 76(6), 957-969
CODEN: BCBIEQ; ISSN: 0829-8211
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 145 refs. The past years have witnessed an increasing no. of reports relative to homeobox genes in endoderm-derived tissues. In this review, we focus on the caudal-related **Cdx-1** and Cdx-2 homeobox genes to give an overview of the in vivo, in vitro, and ex vivo approaches that emphasize their primary role in intestinal development and in the control of intestinal cell proliferation, differentiation, and **identity**. The participation of these genes in colon **tumorigenesis** and their **identification** as important actors of the oncogenic process are also discussed.

REFERENCE COUNT: 146 THERE ARE 146 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:19937 HCAPLUS
DOCUMENT NUMBER: 128:100989
TITLE: Adhesion of neutrophils to epidermal cells: prerequisites for and blocking by anti-CD11b antibodies
AUTHOR(S): Von Den Driesch, P.; Weller, M.; Worl, P.
CORPORATE SOURCE: Department of Dermatology, University of Erlangen Nurnberg, Erlangen, 91052, Germany
SOURCE: Arch. Dermatol. Res. (1997), 289(12), 692-697
CODEN: ADREDL; ISSN: 0340-3696
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immigration of neutrophils into the epidermis is a hallmark of several so-called neutrophilic dermatoses. In this study we used a frozen section adhesion assay to study the impact of different activation procedures as well as of **CD11** integrins on cell-cell adhesion between neutrophils and epidermal cells. Serial sections from punch biopsies of healthy donors were incubated with freshly prepd. neutrophils for 40 min and adherent cells were counter after washing. We found that preactivation of the biopsies with interferon-.gamma. in vitro is a prerequisite for neutrophil binding. Activation of neutrophils with N-formyl-methionyl-leucyl-phenylalanine (fMLP), **tumor** necrosis factor-.alpha. (TNF-.alpha.) or platelet activating factor (PAF) then leads to a three- to sixfold increase in neutrophil adhesion. This enhanced binding could be blocked by anti-CD11b monoclonal antibodies, whereas anti-CD11a and anti-CD11c antibodies exerted no significant effect. At a temp. of 6.degree., 50% inhibition of neutrophil binding was obsd. Complement factor C3 and fibrinogen, known ligands for CD11b/CD18,

could not be **detected** on epidermal cells by immunohistochem. In summary, our study showed that enhanced binding of neutrophils to epidermal sections can be achieved by prestimulation of both the keratinocytes with interferon-.gamma. and the neutrophils with fMLP, TNF-.alpha. and PAF. This adhesion was furthermore revealed to be dependent on the function of the leukocyte integrin CD11b/CD18.

L17 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:728391 HCAPLUS
DOCUMENT NUMBER: 128:21836
TITLE: .beta.2 Integrins (CD11/CD18) promote apoptosis of human neutrophils
AUTHOR(S): Walzog, Barbara; Jeblonski, Frank; Zakrzewicz, Andreas; Gaehtgens, Peter
CORPORATE SOURCE: Department of Physiology, Freie Universitat, Berlin, D-14195, Germany
SOURCE: FASEB J. (1997), 11(13), 1177-1186
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Apoptosis of human polymorphonuclear neutrophils (PMN) is thought to be crit. for the control of the inflammatory process, but the mechanisms underlying its regulation in physiol. settings are still incompletely understood. This study was undertaken to test the hypothesis that the .beta.2 integrin (**CD11**/CD18) family of leukocyte adhesion mols. contributes to the control of activated PMN by up-regulating apoptosis. Apoptosis of isolated human PMN was investigated by (1) anal. of DNA content, (2) **detection** of DNA degrdn., (3) morphol. studies, and (4) measurement of CD16 expression on the cell surface. The authors found that .beta.2 integrins potentiated the **tumor** necrosis factor .alpha. (TNF-.alpha.)-induced apoptosis within 4 and 8 h after stimulation. The effect required aggregation of the .beta.2 integrin Mac-1 (CD11b/CD18), which was induced by antibody crosslinking, and was independent of Fc receptors. An enhancement of apoptosis was also obsd. after migration of PMN through an endothelial cell monolayer. TNF-.alpha.-induced apoptosis as well as potentiation by .beta.2 integrins was prevented by inhibition of tyrosine kinases with herbimycin A or genistein. The present study provides a new model for the regulation of PMN apoptosis by a functional cross-talk between .beta.2 integrins and TNF-.alpha. with a promoting role for the .beta.2 integrins. This mechanism, which allows enhanced elimination of previously emigrated PMN, may be crit. to abate local inflammatory processes in vivo.

L17 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:620952 HCAPLUS
DOCUMENT NUMBER: 127:276739
TITLE: Dendritic type, accessory cells within the mammalian thymic microenvironment. Antigen presentation in the dendritic neuro-endocrine-immune cellular network
AUTHOR(S): Bodey, Bela; Bodey, Bela, Jr.; Kaiser, Hans E.
CORPORATE SOURCE: Department of Pathology, School of Medicine, University of Southern California, Los Angeles, CA,

USA
SOURCE: In Vivo (1997), 11(4), 351-370
CODEN: IVIVE4; ISSN: 0258-851X
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 263 refs. During mammalian ontogenesis, the thymic "pure" endodermal epithelial anlage develops and differentiates into a complex cellular microenvironment. Beginning the 7-8th week of intrauterine development, thymic epithelial cells chemotactically regulate (induce) numerous waves of migration of stem cells into the thymus, including the CD34+, yolk sac derived, committed hematopoietic stem cells. In vitro expts. have established that CD34+ CD38dim human thymocytes differentiate into T lymphocytes when co-cultured with mouse fetal thymic organs. Hematopoietic stem cells for myeloid and thymic stromal dendritic cells (DCs) are present within the minute population of CD34+ progenitors within the mammalian thymus. The common myeloid, DC, natural killer (NK) and T lymphocyte progenitors have also been **identified** within the CD34+ stem cell population in the human thymus. Interactions between the endocrine and immune systems have been reported in various regions of the mammalian body including the anterior pituitary (AP), the skin, and the central (thymus) and peripheral lymphatic system. The network of bone marrow derived DCs is a part of the reticuloendothelial system (RES) and DCs represent the cellular mediators of these regulatory endocrine-immune interactions. Folliculo-stellate cells (FSC) in the AP, Langerhans cells (LCs) in the skin and lymphatic system, "veiled" cells, lympho-dendritic and interdigitating cells (IDCs) in a no. of tissues comprising the lymphatic system are the cell types of the DC meshwork of "professional" antigen presenting cells (APCs). Most of these cells express the immunocytochem. markers S-100, CD1, CD45, CD54, F418, MHC class I and II antigens, Fc and complement receptors. FSCs are non-hormone secreting cells which communicate directly with hormone producing cells, a form of neuro-endocrine-immune regulation. As a result, an attenuation of secretory responses follows stimulation of these cells. FSCs are also the cells in the AP producing interleukin-6 (IL-6), and they have also been **identified** as the interferon-.gamma. responsive elements. FSCs also express lymphatic DC markers, such as DC specific aminopeptidase, leucyl-.beta.-naphthylaminidase, non-specific esterase, MHC class I and II mols. and various other lymphatic immunol. **determinants** [platelet derived growth factor-.alpha. chain (PDGF-.alpha. chain), CD13, CD14 and L25 antigen]. There is strong evidence that such DCs in the AP, and similar ones in the developing thymus and peripheral lymphatic tissue are the components of a powerful "professional" antigen presenting DC network. These APCs contain a specialized late endocytic compartment, MIIC (MHC class II-enriched compartment), that harbors newly synthesized MHC class II antigens en route to the cell membrane. The limiting membrane of MIIC can fuse directly with the cell membrane, resulting in release of newly secreted intracellular MHC class II antigen contg. vesicles (exosomes). DCs possess the ability to present foreign peptides complexed with the MHC mols. expressed on their surfaces to naive and resting T cells. There are a no. of "mol. couples" that influence DC and T lymphocyte interaction during antigen presentation: **CD11**/CD18 integrins, intercellular adhesion mols. (ICAMs), lymphocyte function assocd. antigen 3 (LFA-3), CD40, CD80/B7-1, CD86/B7-2, and heat-stable

antigen. The "mol. couples" are involved in adhesive or co-stimulatory regulations, mediating an effective binding of DCs to T lymphocytes and the stimulation of specific intercellular communications. DCs also provide all of the known co-stimulatory signals required for activation of unprimed T lymphocytes. It has been shown that DCs initiate several immune responses, such as the sensitization of MHC-restricted T lymphocytes, resistance to infections and **neoplasms**, rejection of organ transplants, and the formation of T-dependent antibodies. In addn., DCs and specialized epithelial tissue structures (such as "the nursing" thymic epithelial cells - TNCs) may also be involved in direct, cryptocrine-type cell to cell interactions with the epithelial cells of the thymus. TNCs regulate the development of immature thymocytes into immunocompetent T lymphocytes by emperipolesis, a highly specialized form of cell-cell interaction in which immature thymocytes are engulfed by large thymic reticulo-epithelial (RE) cells. TNCs in vitro are capable of rescuing an early subset of CD4+ CD8+ thymocytes from programmed cell death at 32.degree.C, the temp. at which binding and internalization were **identified**. This thymocyte subpopulation later matured to a characteristic IP at the double pos. stage of T lymphocyte differentiation that is indicative of pos. selection.

L17 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:298349 HCAPLUS
DOCUMENT NUMBER: 127:23717
TITLE: Characterization of cellular response to silicone implants in rats: implications for foreign-body carcinogenesis
AUTHOR(S): James, S. Jill; Pogribna, Marta; Miller, Barbara J.; Bolon, Brad; Muskhelishvili, Levan
CORPORATE SOURCE: Natl. Cent. Toxicolog. Res., FDA, Jefferson, AR, 72079, USA
SOURCE: Biomaterials (1997), 18(9), 667-675
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Foreign-body (FB) **carcinogenesis** is a classic model of multistage **tumor** development in rodents. Previous studies have demonstrated that the phys. characteristics of the implant, and not the chem. compn., are the crit. **determinants** of **tumor** development. The recent controversy over silicone breast implants has raised questions regarding the potential **carcinogenicity** of lifetime tissue exposure to silicone products. The present study was designed to det. whether the inflammatory and fibrotic reactions assocd. with silicone implants are due to a non-specific foreign-body reaction or whether these responses reflect the unique chem. compn. of silicone. F344 rats were implanted s.c. with one of three biomaterials: silicone elastomer (Group 1), impermeable cellulose acetate filters (Group 2, pos. control); or porous cellulose acetate filters (Group 3, neg. control). The silicone and cellulose implants of Groups 1 and 2 have been previously shown to induce fibrosarcomas in rodents, whereas the porous cellulose acetate implants of Group 3 have been shown to be non-**carcinogenic**. One week and two months after implantation, the pericapsular tissues were evaluated using histopathol. and in situ immunohistochem. analyses.

Endpoints included expression of leukocyte antigens CD4 (T helper/inducer), CD8 (T suppressor/cytotoxic) and **CD11** b/c (macrophage), proliferating cell nuclear antigen (PCNA) as an indicator of proliferation, and in situ end-labeling (ISEL) of 3'OH DNA strand breaks as an indicator of DNA damage and apoptosis. The results indicated that the acute and chronic cellular responses to silicone (Group 1) were not different from impermeable cellulose filters (Group 2) of **identical** size and shape, suggesting that these responses were not unique to silicone. The inflammatory response to the **carcinogenic** cellulose and silicone implants (Group 1 and 2) was attenuated and assocd. with the formation of a thick fibrotic capsule. In contrast, the porous cellulose filters (Group 3) induced a markedly different cellular response in which the inflammatory reaction was more extensive, prolonged and assocd. with minimal fibrosis. Within the fibrotic capsule surrounding the **tumorigenic** implants, but not the non-**tumorigenic** implants, cell proliferation and apoptotic cell death were increased and assocd. with persistent DNA strand breaks. Taken together, the results suggest that the micrometer-scale surface morphol. of the implant dets. the nature of the subsequent cellular response which may predispose to **tumor** development. Further, these studies serve to emphasize the crit. importance to appropriate phys. controls in studies designed to evaluate **carcinogenic** or autoimmune manifestations assocd. with silicone implants in order to rule out the contribution of the chronic foreign-body reaction.

L17 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:8581 HCAPLUS
DOCUMENT NUMBER: 126:73194
TITLE: Bombesin may stimulate proliferation of human pancreatic cancer cells through an autocrine pathway
AUTHOR(S): Wang, Qiming J.; Knezetic, Joseph A.; Schally, Andrew V.; Pour, Parviz M.; Adrian, Thomas E.
CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University School of Medicine, Omaha, NE, USA
SOURCE: Int. J. Cancer (1996), 68(4), 528-534
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bombesin is trophic to normal pancreas and acinar cell adenocarcinoma, but its effects on ductal cell **tumors** are undetd. The autocrine growth effects of bombesin on well-differentiated (HPAF, **CD11**) and poorly differentiated (CD18, PANC-1) human ductal pancreatic **cancer** cell lines were investigated. Receptor binding of labeled bombesin was measured in a whole-cell microplate assay. Bombesin prodn. was measured by RIA. Proliferative responses were quantified using the MTT assay. The mRNA for bombesin and its receptor were **identified** by **primer** extension anal. A single class of high-affinity binding sites was **detected** on HPAF and CD18 cells. Similar affinities and high receptor densities were found on the 2 cell lines. Bombesin was secreted by all 4 cell lines during 24-h culture in serum-free media, and its recovery was enhanced in the presence of protease inhibitors. **Primer** extension anal. demonstrated the presence of mRNA for both bombesin and its receptor in HPAF, CD18,

CD11 and PANC-1 cells, even though no functional receptor was found in the latter 2 lines. Bombesin significantly stimulated the proliferation of HPAF and CD18 cells. This trophic effect was inhibited by the specific bombesin antagonist RC-3095. Bombesin may act as an autocrine growth factor in some human pancreatic **cancer** cell lines. Furthermore, other cell lines transcribe mRNA for bombesin receptors but have no functional bombesin receptors, suggesting a genetic or post-translational change in the receptor for these cells. Bombesin may be involved as a growth factor in the development of pancreatic ductal adenocarcinoma in humans. This possible autocrine growth pathway may provide an avenue for therapeutic intervention in this malignant disease.

L17 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:654637 HCAPLUS
DOCUMENT NUMBER: 125:299278
TITLE: Cytokine response of B lymphocytes from splenic lymphoma with villous lymphocytes: Correlation with TNF-RII (p75) and CD11c expression
AUTHOR(S): Treton, D.; Valensi, F.; Troussard, X.; Gras, G.; Flandrin, G.; Galanaud, P.; Richard, Y.
CORPORATE SOURCE: INSERM 131, Institut Paris-Sud sur les Cytokines, Clamart, F-92140, Fr.
SOURCE: Hematol. Cell Ther. (1996), 38(4), 345-352
CODEN: HCTHFA; ISSN: 1430-2772
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied the immunophenotype and the functional reactivity to cytokines of blood cells from eight patients with splenic **lymphoma** with villous lymphocytes (SLVL). Cells from all cases exhibited moderate to high levels of membrane Ig, CD22 and CD40 antigens and light chain restriction (.kappa./.lambda.: 1.7/1). CD44, CD54 and CD11b expression was **detected** in all cases whereas CD11c was expressed in only four cases (50%). CD11c+ cells lacked CD21 and CD23 expression whereas CD11c- cells expressed both these antigens. Cells from most patients (7/8) responded to IL2 whereas only four responded to IL4 and three to TNF.alpha.. The response to TNF.alpha. correlated with spontaneous TNF-RII and CD11c expression. Although two days of culture induced the TNF-RII expression in **CD11**- cells, they remained unresponsive to TNF.alpha.. These two groups of SLVL patients also differed by IL10 mRNA content: the former (CD11c+, TNF-RII+) contained TNF.alpha. and IL10 mRNA whereas the latter (CD11c-, TNF-RII-) lacked IL10 mRNA, even after two days of culture. There were thus two groups of SLVL patients: CD11c+ and CD11c-, exhibiting different patterns of cytokine response and prodn. These groups may correspond to different cell origins or different progression stages of the disease.

L17 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:591176 HCAPLUS
DOCUMENT NUMBER: 125:245336
TITLE: Heat shock and cytokines modulate the expression of adhesion molecules on different human gastric-cancer cell lines
AUTHOR(S): Hsieh, M. -C.; Wu, C. -W.; Wu, L. -H.; Lui, W. -Y.; P'eng, F. -K.; Yu, C. -L.

CORPORATE SOURCE: Department Surgery, Veterans General Hospital, Taipei, 11217, Taiwan
SOURCE: Int. J. Cancer (1996), 67(5), 690-694
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To understand the expression and modulation of adhesion mols. (AMs) on the surface of different gastric **cancers**, we studied 4 gastric-**cancer** cell lines including SC-M1, KATO-III, AGS and AZ-521. The expression of E-cadherin, integrins (.beta.1, .beta.2 and .beta.3), ICAMs (1 and 2), and **CD11** (a, b and c) on the cells was **detected** by flow cytometry. We found that E-cadherin was only expressed on SC-M1 and KATO-III. CD29 (.beta.1 integrin) could be found in cells of all 4 lines. CD54 (ICAM-1) could not be **detected** in AZ-521. In contrast, CD18 (.beta.2 integrin), CD61 (.beta.3 integrin), ICAM-2, CD11a, CD11b and CD11c were all absent from these cells. Heat-shock treatment (42.5.degree., 60 min) enhanced the expression of E-cadherin, CD29 and CD54 on SC-M1, and of CD29 on AGS. In addn., TNF-.alpha. (50U/mL) and IL-1.beta. (10U/mL) modulated the expression of these AMs, like heat-shock treatment. The increment of these adhesion mols. caused by heat shock, TNF-.alpha. and IL-1.beta. stimulation on SC-M1 was also confirmed by Western blot anal. Functionally, these treatments increased the binding between normal human mononuclear cells and SC-M1 cells. The heat-shock treatment could induce a significant amt. of TNF-.alpha. and IL-1.beta. release from SC-M1 and KATO-III, but seemed irrelevant to the expression of AMs. These results suggest that limited adhesion mols. were expressed on the surface of different gastric **cancer** cells. Heat shock, IL-1.beta. and TNF-.alpha. may selectively modulate the expression of these 3 mols. on some of the cells, and this is probably related to their antitumor effect.

L17 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:711743 HCAPLUS
DOCUMENT NUMBER: 123:110112
TITLE: Polymorphonuclear leukocyte migration through human dermal fibroblast monolayers is dependent on both .beta.2-integrin (CD11/CD18) and .beta.1-integrin (CD29) mechanisms
AUTHOR(S): Gao, J. X.; Issekutz, A. C.
CORPORATE SOURCE: Department Pediatrics, Microbiology and Immunology, Dalhousie University, Halifax, NS, Can.
SOURCE: Immunology (1995), 85(3), 485-94
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Accumulation of leukocytes in inflammation involves their migration through vascular endothelium and then in the connective tissue. We investigated human polymorphonuclear leukocyte (PMNL) migration through a biol. barrier of human dermal fibroblasts grown on microporous filters, as a model of PMNL migration in the connective tissue. PMNL did not migrate through a fibroblast monolayer unless a chemotactic factor, e.g. C5a, interleukin-8 (IL-8) or zymosan-activated plasma (ZAP; C5adesArg), was added. This migration was partially inhibited (35-70%, depending on the stimulus) by treatment of PMNL with monoclonal antibody (mAb) to CD18

(.beta.2-integrins). Most of the CD18-independent migration was inhibited by mAb to .beta.1-integrins (CD29). Inhibition by mAb to .beta.1 was obsd. when the PMNL, but not the fibroblasts, were treated with mAb. The role of .beta.1-integrins in PMNL transfibroblast migration was **detectable** only when the function of the **CD11**-CD18 complex was blocked, because mAb to .beta.1-integrin alone had no significant effect on PMNL migration. Migration induced by C5a was more CD18-independent compared to IL-8 or C5adesArg. The CD18-independent migration was also inhibited by mAb to the .beta.1-integrin subunits .alpha.5 (of very late antigens-5; VLA-5) and .alpha.6 (of VLA-6). Treatment of the fibroblasts (4 h) with **tumor** necrosis factor-.alpha. (TNF-.alpha.) or IL-1.alpha. enhanced C5a-induced PMNL transfibroblast migration and increased the proportion of migration utilizing the **CD11**-CD18 mechanism. However, TNF-.alpha. treatment had no effect on the degree of .beta.1-integrin-dependent migration. These findings suggest that in response to the chemotactic factors C5a, IL-8 and C5adesArg, PMNL migration in the connective tissue is mediated by both **CD11**-CD18 (.beta.2) and .beta.1-integrins on the PMNL. The VLA-5 and VLA-6 members of .beta.1-integrins are involved in this process. This is in contrast to PMNL migration across endothelium in this system, which is virtually all CD18 dependent with no significant role for .beta.1-integrins.

L17 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:682349 HCAPLUS
DOCUMENT NUMBER: 123:81465
TITLE: Rapid development of murine AIDS is dependent on signals provided by CD54 and CD11a
AUTHOR(S): Makino, Masahiko; Yoshimatsu, Kazuhiko; Azuma, Miyuki; Okada, Yoshiaki; Hitoshi, Yasumichi; Yagita, Hideo; Takatsu, Kiyoshi; Komuro, Katsutosni
CORPORATE SOURCE: Dep. Bact. Blood Prod., Natl. Inst. Health Japan, Tokyo, Japan
SOURCE: J. Immunol. (1995), 155(2), 974-81
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Murine AIDS (MAIDS) is induced by infection with the replication-defective virus (BM5def) component in the LP-BM5 murine **leukemia** virus (MuLV) mixt. The disease is characterized by polyclonally activated CD4+ T cells and B cells. It is known that BM5def is expressed at highest levels in B lymphocytes and that B cells serve as viral antigen-presenting cells. Full and sustained activation of CD4+ T cells against a conventional antigen (Ag) usually requires both TCR and costimulating signals. Among various mols. known to provide costimulatory function, the expression of CD54 (ICAM-1) and CD11a/CD18 (LFA-1) on MAIDS B cells was increased, whereas that of CD2, heat-stable Ag (CD24), CD80 (B7-1), and CD86 (B7-2) was unchanged from normal. C57BL/6 mice depleted of both CD54 and CD11a expression as a result of chronic administration of mAb developed no MAIDS at 4 wk and 8 wk after LP-BM5 MuLV infection. In addn., the proliferative response of B cells to mitogen was well conserved, whereas MAIDS-assocd. increases in serum Ig levels were inhibited. Replication of BM5def was suppressed markedly in infected mice treated with the CD54 and **CD11** a mAbs. Thus, the CD54/CD11a

signal transduction pathway is a crit. **determinant** of MAIDS development, and the lack of an immune response against viral Ag is enough to suppress BM5def replication and to prevent MAIDS.

L17 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:512012 HCAPLUS
DOCUMENT NUMBER: 122:263496
TITLE: CD11/CD18-independent transendothelial migration of human polymorphonuclear leukocytes and monocytes: involvement of distinct and unique mechanisms
AUTHOR(S): Issekutz, Andrew C.; Chuluyan, H. Eduardo; Lopes, Nancy
CORPORATE SOURCE: Deps. Pediatr., Microbiol.-Immunol., Dalhousie Univ., Halifax, NS, Can.
SOURCE: J. Leukocyte Biol. (1995), 57(4), 553-61
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monocytes and polymorphonuclear leukocytes (PMNLs) migrate across cytokine (interleukin-1, **tumor** necrosis factor) activated endothelium or unstimulated endothelium in response to chemotactic factors in vitro and in vivo utilizing the **CD11**/CD18 (i.e., .beta.2 integrin) adhesion mol. complex. However, in vivo studies have suggested that under some conditions and/or in certain tissues, leukocyte migration can also proceed via **CD11**/CD18-independent mechanisms. Here the authors compared adhesion mechanisms involved in the migration of 51Cr-labeled blood monocytes and PMNLs across human umbilical vein endothelium (HUVE) monolayers. The authors obsd. that monocyte transendothelial migration was not inhibited by monoclonal antibody (mAb) to CD18, when the HUVE was activated with IL-1 and the chemotactic factor C5a induced the migration. This CD18-independent monocyte migration was blocked by treatment of the monocyte with mAb to .beta.1 or .alpha.4 integrin, suggesting that very late activation antigen 4 (VLA-4) on the monocyte served as the alternative migration mechanism. In contrast to monocytes, mAb to CD18 inhibited PMNL migration to C5a across IL-1-activated HUVE, but only by 66%, significantly less than with C5a alone (84%) or IL-1-activated HUVE alone (95%). The migration of anti-CD18 mAb-treated PMNLs was not inhibited by function-blocking mAbs to sialyl Lewisx, L-selectin, .beta.1 or .alpha.4 integrin, the .beta.3-related leukocyte response integrin, IL-8, or platelet-activating factor (PAF) antagonists, alone or in combination. Antibody-blocking studies of the ligands on HUVE indicated that E-selectin may be partially involved in this CD18-independent PMNL migration but that ICAM-1, VCAM-1, PECAM-1, and P-selectin are not involved. Of several chemotactic factors tested, C5a and C5adesArg in activated plasma were the most active in inducing CD18-independent migration of PMNLs across IL-1-activated HUVE. These results demonstrate that (1) monocytes can utilize VLA-4 for optimal transendothelial migration and (2) PMNLs may have a novel CD18-independent migration mechanism that is activated by C5a in conjunction with one or more ligands on cytokine-activated endothelium. This may involve, in part, E-selectin interacting with a yet to be **identified** counter-receptor on PMNLs.

L17 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:411475 HCAPLUS
DOCUMENT NUMBER: 122:185296
TITLE: Lipoxygenase product formation and cell adhesion during neutrophil-glomerular endothelial cell interaction
AUTHOR(S): Brady, Hugh R.; Lamas, Santiago; Papayianni, Aikaterina; Takata, Shoichiro; Matsubara, Mitsunobu; Marsden, Philip A.
CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Harvard Medical Sch., Boston, MA, 02132, USA
SOURCE: Am. J. Physiol. (1995), 268(1, Pt. 2), F1-F12
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leukotriene (LT) and lipoxin (LX) levels were monitored in ionophore-stimulated coincubations of polymorphonuclear neutrophils (PMN) and microvascular kidney glomerular endothelial cells (GEN) to det. the profile of lipoxygenase (LO) products generated during cell-cell interactions and the relative contributions of transcellular pathways to LO product biosynthesis in this setting. LTB4 and LTC4 were the major products formed, as detd. by reverse-phase high-performance liq. chromatog. and RIA. LTB4 and LTC4 levels were increased by 23 and 185%, resp., in coincubations of PMN and GEN, compared with incubations of PMN alone. In contrast, LXA4 and LXB4 levels were not changed in the presence of GEN. These data suggested that GEN utilize PMN-derived LTA4 to generate LT. In keeping with this hypothesis, LT biosynthesis was enhanced if PMN were primed with human granulocyte-macrophage colony-stimulating factor (GM-CSF), a cytokine that augments LTA4 biosynthesis by activated PMN. The influence of LT on PMN adhesion to GEN was also assessed, since adhesion appears to be a pivotal event in recruitment of PMN in acute glomerulonephritis. Under basal conditions, LTB4 provoked low levels of adhesion via a PMN-directed **CD11**/CD18-dependent mechanism. The level of adhesion was markedly enhanced by prior priming of PMN with GM-CSF or activation of GEN with **tumor** necrosis factor-.alpha. (TNF). LTB4 was as potent in this regard as the complement component C5a, platelet-activating factor (PAF), and interleukin-8 (IL-8), other mediators that contribute to the entrapment of PMN in inflamed glomeruli. LTC4 also provoked PMN-GEN adhesion via a **CD11**/CD18-dependent mechanism, but, in contrast to LTB4, via actions with GEN. This action of LTC4 appeared to be mediated, at least in part, by induction of PAF synthesis by GEN. Interestingly, LT-induced PMN-GEN adhesion was markedly attenuated following remodeling of PMN phospholipids with 15(S)-hydroxyeicosatetraenoic acid, a product of 15-LO, which has been implicated as an anti-inflammatory eicosanoid in some exptl. and human inflammatory diseases. Taken together, these results provide further evidence that 1) transcellular biosynthetic pathways may **amplify** the profiles of inflammatory mediators and thereby contribute to leukocyte recruitment in acute glomerulonephritis and 2) to leukocyte recruitment in acute glomerulonephritis and 2) that products of the 5-LO and 15-LO pathways may exert opposing actions on PMN trafficking during glomerular inflammation in vivo.

L17 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:602792 HCAPLUS

DOCUMENT NUMBER: 121:202792
TITLE: Altered expression of CD11/CD18 on the peripheral blood phagocytes of patients with tuberculosis
AUTHOR(S): Yassin, R. J.; Hamblin, A. S.
CORPORATE SOURCE: Department of Immunology, UMDS, London, UK
SOURCE: Clin. Exp. Immunol. (1994), 97(1), 120-5
CODEN: CEXIAL; ISSN: 0009-9104
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tuberculosis (TB), caused by Mycobacterium tuberculosis, is characterized by granulomatous lesions made up of epithelioid cells, giant cells and mononuclear leukocytes. Cell-cell adhesion is important in granuloma formation and in the leukocyte migration which accompanies it. We have recently shown increased expression of the adhesion mols. **CD11**/CD18 (LeuCAMs, .beta.2 integrins) on peripheral blood leukocytes from patients with sarcoidosis (Shakoor & Hamblin, 1992). Here we have studied the expression of **CD11**/CD18 and CD29 (VLA .beta.1 integrin) on the peripheral blood leukocytes of 10 TB patients by flow cytometry. The d. (expressed as mean fluorescence intensity) of CD11b on monocytes and polymorphs was increased, as was CD11c and CD18 on polymorphs. CD11a expression was significantly reduced on polymorphs. No differences were found in the expression of CD29, the percentages of cells expressing any mol. and, in contrast to sarcoidosis, the d. of any mol. on lymphocytes. Although the cytokine **tumor** necrosis factor (TNF) has been implicated in the process of up-regulation, an ELISA for TNF failed to **detect** significant levels in plasma. The results suggest increased peripheral phagocyte **CD11**/CD18 expression is a feature of TB, which may contribute to the pathol. processes involved.

L17 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:189511 HCAPLUS
DOCUMENT NUMBER: 120:189511
TITLE: Leukemia-associated marker combinations in acute leukemia suitable for **detection** of minimal residual disease
AUTHOR(S): Babusikova, O.; Mesarosova, A.; Konikova, M.; Kusenda, J.; Glasova, M.; Klobusicka, M.
CORPORATE SOURCE: Cancer Res. Inst., Slovak Acad. Sci., Bratislava, 812 32, Slovakia
SOURCE: Neoplasma (1993), 40(5), 275-81
CODEN: NEOLA4; ISSN: 0028-2685
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antigen combinations were **identified** in **leukemia** cells that are absent or extremely rare among normal hemopoietic cells. Some of the combinations related to the simultaneous surface and cytoplasmic marker expression, others, expressed mainly on cell surface membrane, represented atypical or aberrant combinations. Comparing membrane (m) and cytoplasmic (c) antigen expression (followed in 23 acute **leukemia** cases), the authors obsd. that CD3 could be **detected** in cytoplasm in the majority of T-ALL cells, while it was absent on cell surface membrane, where simultaneous expression of more immature T cell markers, such as CD7 and CD5, could be **detected**. Combination of mCD7/cCD3 could be regarded as a suitable marker of individual T-ALL

cells. In cases of B-precursors of acute **leukemia** cells, a **leukemia**-related combination of mCD19/cCD22 was found, which could characterize a single **leukemia** cell. The cells in one of 11 AML cases were pos. for CD13 in cytoplasm, but not on cell surface membrane. The cells in another two AML cases were pos. for **CD11** in cytoplasm but not on cell surface membrane, where CD13 or CD33 were expressed. Again, marker combinations of mCD33/cCD13 and mCD13 or mCD33/cCD11, resp., represent a **leukemia**-related feature, suitable for tracing single **leukemia** cells in double immunofluorescence. Acute **leukemia** defined by the coexpression on most blast cells of antigens classically attributed to different lineages (referred as atypical/aberrant marker combinations) remains a rare event. In summary, 44 of 50 cases (88%) from this acute **leukemia** series allowed the **detection** of minimal residual disease.

L17 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:103606 HCAPLUS
DOCUMENT NUMBER: 120:103606
TITLE: Comparison of p53 protein expression and cellular localization in human and hamster pancreatic cancer cell lines
AUTHOR(S): Mogaki, Masatoshi; Hirota, Masahiko; Chaney, William G.; Pour, Parviz M.
CORPORATE SOURCE: Eppley Inst. Res. Cancer Allied Dis., Univ. Nebraska Med. Cent., Omaha, NE, 68198-6805, USA
SOURCE: Carcinogenesis (1993), 14(12), 2589-94
CODEN: CRNGDP; ISSN: 0143-3334
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors compared the expression of p53 protein in four human pancreatic **cancer** cell lines (HPAF, **CD11**, CD18 and PANC-1) and four hamster pancreatic **cancer** cell lines (PC-1, PC-1.2, PC-1.0 and H2T) by the monoclonal antibodies PAb421 and PAb240. All human pancreatic **cancer** cell lines, but not the hamster cells, reacted with pAb421. All human and hamster pancreatic **cancer** cell lines reacted with pAb240 upon immunoblotting and in immunocytochem. However, immunopptn. with PAb240 was **detected** only in human cell lines HPAF, **CD11**, and CD18 cells but not in PANC-1 or in any of the hamster cell lines. During exponential growth, immunoreactivity was **detected** mainly in the nucleus of PC-1, PC-1.2 and PANC-1 cells (nuclear type) and in both the nucleus and the cytoplasm of PC-1.0, H2T, HPAF, **CD11**, and CD18 cells (diffuse type). At confluence, the expression of p53 was decreased in most of the human cell lines as was proliferative cell nuclear antigen. After incubation with 1 mM hydroxyurea, cells with nuclear p53 expression did not show an altered cellular distribution of p53 protein, whereas cells with a diffuse type of localization pattern showed an increase in the nuclear staining. Cytoplasmic immunoreactivity was found in PC-1.0, PC-1, PC-1.2, HPAF, **CD11** and CD18 cells that were treated with 100 ng/mL of nocodazole. After heat stress with 1 h incubation at 42.degree., p53 protein was **detected** in the cytoplasm and nucleolus of all cell lines. After 24-48 h incubation at 37.degree., this change in cellular distribution of p53 in response to heat stress was reverted to a

preheat stress pattern. The overall results suggest that neither the p53 of PANC-1 nor the hamster pancreatic **cancer** cell lines are immunopptd. with the PAb240. Apparently, cell cycle and heat stress are two of the factors that influence cellular localization of p53 protein in both human and hamster pancreatic **cancer** cells.

L17 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:656537 HCAPLUS
DOCUMENT NUMBER: 119:256537
TITLE: Diagnostic and/or therapeutic immunoconjugates targeted to neovascular endothelial cells
INVENTOR(S): Thorpe, Philip E.; Burrows, Francis J.
PATENT ASSIGNEE(S): University of Texas System, USA; Imperial Cancer Research Technology
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317715	A1	19930916	WO 1993-US1956	19930305
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337378	A1	19931005	AU 1993-37378	19930305
EP 627940	A1	19941214	EP 1993-906289	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6004554	A	19991221	US 1994-295868	19941202
PRIORITY APPLN. INFO.:			US 1992-846349 A2	19920305
			WO 1993-US1956 A	19930305

AB An antibody or antibody fragment that recognizes a cell surface antigen assocd. with endothelial vasculature of a vascularized tumor mass is linked to a therapeutic or diagnostic agent for treatment or diagnosis of vascularized tumors. The antibody may be linked to a paramagnetic or radioactive ion, cytotoxic agent, cytokine, etc. Thus, a neuroblastoma transfected with the mouse .gamma.-interferon gene was grown in mice with severe combined immunodeficiency. The .gamma.-interferon secreted by the tumor induced expression of MHC class II antigens on the tumor vascular endothelium. A rat IgG2b monoclonal antibody which recognized MHC Ia antigens, conjugated to deglycosylated ricin A chain, was used successfully for treatment of the neuroblastoma.

L17 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:426502 HCAPLUS
DOCUMENT NUMBER: 119:26502
TITLE: Phorbol ester-induced degranulation in adherent human eosinophil granulocytes is dependent on CD11/CD18 leukocyte integrins
AUTHOR(S): Egesten, Arne; Gullberg, Urban; Olsson, Inge; Richter,

Johan
CORPORATE SOURCE: Dep. Med., Univ. Lund, Lund, Swed.
SOURCE: J. Leukocyte Biol. (1993), 53(3), 287-93
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Secretion of unique eosinophil granule constituents may play a role in allergic and parasitic reactions. Therefore, tho authors have investigated possible mechanisms for regulation of secretion in eosinophils. A hemolytic plaque assay and an enzyme-linked immunospot (ELISPOT) assay were developed for **detection** of secreted eosinophil cationic protein (ECP) from single adherent eosinophils. The protein kinase C activator phorbol 12-myristate 13-acetate (PMA) induced release of ECP in a dose-dependent fashion but 4-.alpha.-PMA, an analog that does not activate protein kinase C, did not cause degranulation. Staurosporine and K 252a, inhibitors of protein kinase C, decreased PMA-induced ECP secretion. Low concns. of cytochalasin B enhanced PMA-induced secretion but high concns. had an inhibitory effect. The calcium ionophores A 23187 and ionomycin were weaker secretagogues than PMA. **Tumor** necrosis factor, granulocyte-macrophage colony-stimulating factor, interleukin-3, interleukin-5, N-formylmethionyl-leucyl-phenylalanine, and lipopolysaccharide caused little or no degranulation in adherent eosinophils. Preincubation of eosinophils with antibodies to CD18, the common .beta. chain of leukocyte adhesion proteins, resulted in inhibition of PMA-induced ECP release from adherent cells. BAPTA, an agent that acts intracellularly by chelation of calcium, also inhibited PMA-mediated ECP release. In conclusion, PMA induces release of ECP from single adherent eosinophils and the effect appears to be mediated via protein kinase C and, in contrast to that in neutrophils, to be dependent on **CD11**/CD18 leukocyte integrins.

L17 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:167361 HCAPLUS
DOCUMENT NUMBER: 118:167361
TITLE: Human colon cancer cells express ICAM-1 in vivo and support LFA-1-dependent lymphocyte adhesion in vitro
AUTHOR(S): Kelly, Ciaran P.; O'Keane, J. Conor; Orellana, Jose; Schroy, Paul C., III; Yang, Shi; LaMont, J. Thomas; Brady, Hugh R.
CORPORATE SOURCE: Sch. Med., Boston Univ., Boston, MA, 02118, USA
SOURCE: Am. J. Physiol. (1992), 263(6, Pt. 1), G864-G870
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intercellular adhesion mol.-1 (ICAM-1) is a cell surface adhesion glycoprotein that mediates leukocyte adhesion through interaction with the leukocyte **CD11**/CD18 adhesion complex. The aim of this study was to det. whether ICAM-1 is expressed by normal or neoplastic colonic epithelial cells. Immunohistochem. studies on human colonic tissue demonstrated focal ICAM-1 expression by colonic **carcinomas** but not by normal colonic epithelium. ICAM-1 expression by colonic **carcinomas** showed a pos. correlation with the presence of a peritumoral inflammatory infiltrate. Surface expression of ICAM-1 was also obsd. in HT-29 cultured human colon **cancer** cells by both

immunohistochem. and enzyme **immunoassay**. Interferon-.gamma. and interleukin-1.beta. increased ICAM-1 surface expression by HT-29 cells in a dose-dependent manner. Upregulation of ICAM-1 surface expression became evident some hours after cytokine stimulation and was inhibited by both actinomycin D and cycloheximide, indicating a requirement for de novo RNA and protein synthesis. HT-29 monolayers supported adhesion of human lymphocytes as detd. by a quant. 111In-labeled leukocyte adhesion assay. Adhesion was mediated in part via interaction of ICAM-1 on HT-29 cells with lymphocyte function-assocd. antigen-1 (CD11a/CD18) on lymphocytes, as defined by using blocking monoclonal antibodies. Expression of ICAM-1 and/or other leukocyte adhesion receptors by neoplastic epithelial cells may play a role in directing leukocyte trafficking and leukocyte-epithelial cell interactions in colonic **carcinoma**.

L17 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:166353 HCAPLUS
DOCUMENT NUMBER: 118:166353
TITLE: Production of scatter factor-like activity by a nitrosamine-induced pancreatic cancer cell line
AUTHOR(S): Hirota, Masahiko; Egami, Hiroshi; Corra, Stefano; Fujii, Hideki; Chaney, William G.; Rizzino, Angie; Pour, Parviz M.
CORPORATE SOURCE: Eppley Inst. Res. Cancer allied Dis., Univ. Nebraska, Omaha, NE, 68198-6805, USA
SOURCE: Carcinogenesis (London) (1993), 14(2), 259-64
CODEN: CRNGDP; ISSN: 0143-3334
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two hamster pancreatic **cancer** cell lines, PC-1 and PC1.0, established from N-nitrosobis(2-oxopropyl)amine-induced pancreatic ductal/ductular adenocarcinomas exhibit different growth patterns. PC-1 cells, which produce well differentiated adenocarcinomas in vitro after allogeneic inoculation, form cell aggregates and characteristic island-like structures in vitro. PC1.0 cells, which produce poorly differentiated **tumors** in vivo, form dispersed colonies in vitro. Conditioned medium prepd. from PC1.0 cells inhibits PC-1 cells from forming island-like colonies. The conditioned medium also prevents several human pancreatic **carcinoma** cell lines, HPAF, **CD11** and CD18, from forming compact colonies. These properties are similar to those described previously as scatter factors. The scatter factor-like activity is heat-labile, acid-stable, non-dialyzable, trypsin sensitive and unaffected by reducing agents. The activity is not suppressed by addn. of heparin, and it does not bind to heparin. In addn., the scatter phenomenon is not reproduced by acidic or basic fibroblast growth factor, epidermal growth factor or transforming growth factor-.beta.1. Based on these findings, it appears that the scattering activity produced by PC1.0 cells differs from the scatter factors that have been **identified** in other systems.

L17 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:212789 HCAPLUS
DOCUMENT NUMBER: 116:212789
TITLE: Absolute requirement of **CD11**/CD18 adhesion molecules, FcRII, and the phosphatidylinositol-linked

FcRIII for monoclonal antibody-mediated neutrophil antihuman **tumor** cytotoxicity
AUTHOR(S): Kushner, Brian H.; Cheung, Nai Kong V.
CORPORATE SOURCE: Dep. Pediatr., Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SOURCE: Blood (1992), 79(6), 1484-90
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was previously shown that 3F8, a murine IgG3 monoclonal antibody (MoAb) specific for the ganglioside GD2, mediates **tumor** cell kill in vitro and in vivo. Here, receptor requirements are described for polymorphonuclear leukocytes (PMN) in 3F8-mediated cytotoxicity (ADCC) of human GD2(+) **melanoma** and neuroblastoma cell lines. PMN from a child with leukocyte adhesion deficiency (LAD) were devoid of **CD11** /CD18 adhesion mols. and mounted no **detectable** ADCC. MoAb to CD11b, CD11c, and CD18 each efficiently blocked ADCC by normal PMN. In contrast, a panel of different MoAbs to CD11a had no inhibitory effect on ADCC, a finding consistent with the low-to-absent expression of the CD11a ligand, intercellular adhesion mol.-1, on the target cells. Granulocyte-macrophage colony-stimulating factor (GM-CSF) significantly increased the expression of CD11b, CD11c, and CD18 on normal PMN, decreased the expression of Fc receptors (FcR), and enhanced ADCC by normal but not by LAD PMN. MoAbs to FcRII and FcRIII each efficiently blocked ADCC; anti-FcRI MoAb had no effect. Flow cytometry using anti-FcRII MoAb vs. anti-FcRIII MoAb did not show cross competition, suggesting that inhibition of ADCC was not a steric effect resulting from FcRII proximity to FcRIII. PMN deficient in FcRIII (obtained from patients with paroxysmal nocturnal hemoglobinuria) and PMN depleted of FcRIII by treatment with elastase or phosphatidylinositol (PI)-specific phospholipase C produced low ADCC, supporting a role for the PI-linked FcRIII. Thus, optimal ADCC using human PMN, human solid **tumor** cells, and a clin. active MoAb (conditions that contrast with the heterologous antibodies and nonhuman or nonneoplastic targets used in most models of PMN ADCC) required CD11b, CD11c, FcRII, and the PI-linked FcRIII. Furthermore, in this clin. relevant system, GM-CSF enhancement of antitumor PMN ADCC correlated with increased expression of **CD11** /CD18 mols.

L17 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:104104 HCAPLUS
DOCUMENT NUMBER: 116:104104
TITLE: Selective up-regulation of human granulocyte integrins and complement receptor 1 by cytokines
AUTHOR(S): Limb, G. A.; Hamblin, A. S.; Wolstencroft, R. A.; Dumonde, D. C.
CORPORATE SOURCE: Rayne Inst., St. Thomas' Hosp., London, SE1 7EH, UK
SOURCE: Immunology (1991), 74(4), 696-702
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The percentage of human granulocytes expressing the integrins CD11b and CD11c as well as complement receptor 1 (CD35) was increased by short-term incubation of whole blood with interleukin-2 (IL-2), IL-4 and

tumor necrosis factors alpha and beta (TNF-.alpha. and TNF-.beta.). The mean fluorescence intensity of granulocyte CD18 was also increased by the above cytokines, while that of CD11b was only increased by TNF-.alpha.. Up-regulation of granulocyte CD18 expression was seen with 1 U/mL of IL-2, TNF-.alpha. or TNF-.beta., in contrast to the effect of IL-4 which was only obsd. with 100 U/mL. Similarly, enhanced expression of CD35 was induced by 1 U/mL of IL-2 or TNF-.alpha. but not by concns. of IL-4 or TNF-.beta. <100 U/mL. Cytokine effects on the **CD11**/CD18 complex and CD35 mols. were not modified by cycloheximide, suggesting that their increased expression was not due simply to synthesis de novo. None of the granulocyte surface **determinants** investigated was altered upon short-term incubation of blood with either IL-1, IL-6 or interferon-.gamma.. The demonstration in vitro that cytokines selectively up-regulate granulocyte integrins and complement receptor 1 suggests that similar mechanisms may be operating during the control of granulocyte-mediated inflammatory processes.

L17 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:5129 HCAPLUS
DOCUMENT NUMBER: 116:5129
TITLE: Involvement of leukocyte (.beta.2) integrins (CD18/**CD11**) in human monocyte **tumoricidal** activity
AUTHOR(S): Bernasconi, Sergio; Peri, Giuseppe; Sironi, Marina; Mantovani, Alberto
CORPORATE SOURCE: Ist. Ric. Farmacol. "Mario Negri", Milan, 20157, Italy
SOURCE: Int. J. Cancer (1991), 49(2), 267-73
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Appropriately activated mononuclear phagocytes mediate contact-dependent **tumoricidal** activity. Adhesion structures involved in contact-dependent **tumor** cytotoxicity have not been defined. This study was aimed at **identifying** the adhesion structures involved in the **tumoricidal** activity of activated (IFN-.gamma. + LPS) human monocytes. **Tumor** cells of different histol. origin were used as targets in a 48-h cytolysis assay. Anti-CD18 (integrin .beta.2 chain) monoclonal antibodies (MAbs) substantially (50-80%) inhibited human monocyte cytotoxicity. When the role of different .alpha.-chains was studied, anti-.alpha.L (CD11a, LFA1), anti-.alpha.M (CD11b, Mac-1), and anti-.alpha.X (CD11c, p150,95) caused marginal inhibition, but the effect of the 3 combined was comparable to that of anti-CD18. Anti-CD18 MAb did not affect the release of various cytotoxic mols. (e.g. TNF) by activated human monocytes. Activated monocytes showed augmented binding to target cells and anti-CD18 MAb inhibited the binding of resting and activated monocytes to **tumor** target cells. While INF-.gamma. alone augmented expression of leukocyte integrins and LPS had no effect, the 2 activation signals, combined for optimal stimulation of **tumoricidal** activity, resulted in no appreciable increase in these leukocyte adhesion mols., as assessed by flow cytometry. Thus, the augmented CD18-dependent binding of activated monocytes on **tumor** cells depends mainly upon changes in the adhesive properties of these mols. rather than upon increased nos. on the cell surface. Anti-ICAM-1 MAb reduced monocyte cytotoxicity on **tumor** cells, which is

consistent with a role of the **CD11**/CD18 adhesion pathway. These results implicate activated leukocyte (.beta.2) integrins (**CD11**/CD18) as important adhesion mols. in the contact-dependent **tumoricidal** activity of human monocytes.

L17 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:1496 HCAPLUS
DOCUMENT NUMBER: 116:1496
TITLE: Molecular cloning and sequence analysis of the human ribosomal protein S16
AUTHOR(S): Batra, Surinder K.; Metzgar, Richard S.; Hollingsworth, Michael A.
CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA
SOURCE: J. Biol. Chem. (1991), 266(11), 6830-3
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cDNA library from a poorly differentiated human pancreatic **tumor** cell line was **screened** for differentially expressed mRNAs using single-stranded cDNA probes synthesized from poly(A+) RNA of the poorly differentiated cell line Panc 1 and a very well differentiated cell line **CD11**. One of the cDNA clones isolated hybridized to a transcript size of 650 base pairs on Northern blot anal. and showed 30-fold higher expression in the poorly differentiated cell line as compared with the well differentiated cell line. Sequence anal. of this cDNA clone and its deduced amino acid sequence showed an open reading frame of 441 nucleotides with 100 and 98.6% homol. to ribosomal protein S16 (rpS16) from rat and mouse, resp. Northern blot analyses with a panel of 14 pancreatic cell lines, 2 breast cell lines, 2 colon cell lines, and several other tissues showed higher expression of rpS16 only in the poorly differentiated pancreatic **tumor** cell line Panc 1. The expression of mRNA for 2 other ribosomal proteins, rpL30 and prL32, were not elevated in Panc 1. Southern blot anal. of genomic DNA showed a 20-fold **amplification** of a single band among the rpS16 family only in the Panc 1 cell line.

L17 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:512620 HCAPLUS
DOCUMENT NUMBER: 115:112620
TITLE: Mechanisms of eosinophil adherence to cultured vascular endothelial cells. Eosinophils bind to the cytokine-induced endothelial ligand vascular cell adhesion molecule-1 via the very late activation antigen-4 integrin receptor
AUTHOR(S): Dobrina, A.; Menegazzi, R.; Carlos, T. M.; Nardon, E.; Cramer, R.; Zacchi, T.; Harlan, J. M.; Patriarca, P.
CORPORATE SOURCE: Inst. Gen. Pathol., Univ. Trieste, Trieste, 34127, Italy
SOURCE: J. Clin. Invest. (1991), 88(1), 20-6
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanisms involved in the adherence of normal peripheral blood eosinophils to cultured human umbilical vein endothelial cells (HEC) were

examd. under 3 conditions: (a) adherence in the absence of treatment of HEC or eosinophils with activating agents (basal adherence); (b) adherence induced by stimulation of eosinophils with phorbol ester (eosinophil-dependent adherence); and (c) adherence induced by pretreatment of HEC with LPS, **tumor** necrosis factor (TNF), or IL-1 (endothelial-dependent adherence). A mechanism was **identified** that was equally active in basal, eosinophil-dependent, and endothelial-dependent adherence. This mechanism was optimally active in the presence of both Ca2+ and Mg2+, and reduced in the presence of Ca2+ only or Mg2+ only. A second mechanism of adherence was involved in eosinophil- and in endothelial-dependent adherence. This mechanism was dependent on the **CD11**/CD18 adhesion complex of eosinophils and it was active in the presence of Ca2+ and Mg2+ or Mg2+ only, but not Ca2+ only. The third mechanism of adherence was specific for endothelial-dependent adherence. It involved the endothelial ligand vascular cell adhesion mol.-1 (VCAM-1) and the eosinophil receptor very late activation antigen-4 (VLA-4, CD49d/CD29). This mechanism was active in the presence of Ca2+ and Mg2+ but not of Ca2+ only or Mg2+ only, and was not up- or downregulated when eosinophils were stimulated with phorbol ester. In contrast, the endothelial leukocyte adhesion mol.-1 (ELAM-1), that binds neutrophils and monocytes, was not involved in eosinophil adherence to LPS-, TNF-, or IL-1-stimulated HEC (i.e., not inhibited by anti-ELAM-1 MAb). Thus, eosinophils, like monocytes and lymphocytes, bind to the cytokine-induced endothelial ligand VCAM-1 via the integrin receptor VLA-4.

L17 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:490384 HCAPLUS
DOCUMENT NUMBER: 115:90384
TITLE: Expression, distribution, and biochemistry of human CD39. Role in activation-associated homotypic adhesion of lymphocytes
AUTHOR(S): Kansas, Geoffrey S.; Wood, Gary S.; Tedder, Thomas F.
CORPORATE SOURCE: Div. Tumor Immunol., Dana-Farber Cancer Inst., Boston, MA, 02115, USA
SOURCE: J. Immunol. (1991), 146(7), 2235-44
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The distribution, biochem. properties, and function of CD39 were characterized with the use of a new mAb termed 400. CD39 is an acidic (isoelec. point, .apprx.4.2) glycoprotein of mol. wt. .apprx.78,000, contg. .apprx.24 kDa of N-linked oligosaccharide but no **detectable** O-linked sugars. CD39 was not expressed by resting blood T, B, or NK cells, neutrophils, or monocytes, but was expressed on activated NK cells, B cells, subsets of T cells, and T cell clones. Furthermore, the pattern of expression of CD39 was distinct from the classic activation antigens CD25 and CD71, inasmuch as it was expressed long after expression of CD25 and CD71 had returned to basal levels. CD39 was easily **detectable** on EBV-transformed B cell lines but was absent from pre-B and non-EBV-transformed B cell lines, most myeloid cell lines, and **leukemic** T cell lines. In lymphoid tissues, germinal center cells expressed little or no CD39, whereas some paracortical lymphocytes and most macrophages and dendritic cells were pos. CD39 was strongly

expressed by endothelium in all tissues examd., including skin, and was present on some, but not all, endothelial cell lines propagated in vitro. Interestingly, mAb binding to certain epitopes on CD39 induced rapid homotypic adhesion that appeared to involve LFA-1 (CD11a/CD18), but was morphol. and kinetically distinct from that induced by PMA. Anti-CD39 mAb also induced homotypic adhesion in an **CD11**/CD18-EBV-transformed B cell line derived from a patient with severe leukocyte adhesion deficiency. This adhesion was unaffected by EDTA, suggesting that this pathway of anti-CD39-induced homotypic adhesion was not mediated by any of the known integrins. Apparently, CD39 is involved in the cellular signaling that regulates adhesion.

L17 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:457012 HCAPLUS
DOCUMENT NUMBER: 113:57012
TITLE: **Identification** of surface proteins mediating adherence of CD11/CD18-deficient lymphoblastoid cells to cultured human endothelium
AUTHOR(S): Schwartz, Barbara R.; Wayner, Elizabeth A.; Carlos, Timothy M.; Ochs, Hans D.; Harlan, John M.
CORPORATE SOURCE: Dep. Med., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: J. Clin. Invest. (1990), 85(6), 2019-22
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with severe form of leukocyte adhesion deficiency syndrome do not express the **CD11**/CD18 adhesion complex on any of their leukocytes. Nevertheless, their lymphocytes, unlike their phagocytes, emigrate to extravascular sites of inflammation, demonstrating that surface proteins other than **CD11**/CD18 can mediate lymphocyte adherence to endothelium. Using a B-lymphoblastoid cell line (B-LCL) established from a **CD11**/CD18-deficient patient and cultured human umbilical vein endothelial cells (HEC), the **CD11** /CD18-independent mechanism(s) of lymphocyte adherence to endothelium were investigated. Monoclonal antibodies directed to the .alpha.4 polypeptide (CD49d) and the .beta.1 polypeptide (CD29) of the lymphocyte VLA-4 integrin receptor (CD49d/CD29), and to vascular cell adhesion mol.-1 (VCAM-1) on the endothelial cell significantly inhibited the adherence of the **CD11**/CD18-deficient B-LCL to untreated HEC and to HEC treated with recombinant human **tumor** necrosis factor-.alpha.. Thus, the interaction of the lymphocyte receptor VLA-4 with the endothelial ligand VCAM-1 induced by cytokines at sites of inflammation or immune reaction represents a **CD11**/ CD18-independent pathway of lymphocyte emigration.

L17 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:176577 HCAPLUS
DOCUMENT NUMBER: 112:176577
TITLE: Role of CD18 in lymphokine activated killer (LAK) cell-mediated lysis of human monocytes: comparison with other LAK targets
AUTHOR(S): Blanchard, D. Kay; Hall, Robert E.; Djeu, Julie Y.
CORPORATE SOURCE: Coll. Med., Univ. South Florida, Tampa, FL, 33612, USA
SOURCE: Int. J. Cancer (1990), 45(2), 312-19

CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of CD18, **identified** as the beta chain of the **CD11** family of adhesion glycoproteins, in the lysis of normal autologous monocytes by interleukin-2-activated killer (LAK) cells was explored. The addn. of several prepns. of anti-CD18 monoclonal antibodies (MAbs) to the incubation mixt. of LAK cells and various target cells indicated that lysis of autologous monocytes, K562 erythroleukemia **tumor** cells, FMEX **melanoma tumor** cells, and fresh ovarian **tumor** cells were readily inhibited by all anti-CD18 antibodies tested. Kinetic expts. demonstrated that significant inhibition of lysis occurred if RHI-38 antibody was added up to 2 h after LAK cells were added to target cells. By the use of selective coating of targets and effector cells with RHI-38, it was detd. that anti-CD18 antibody inhibited lysis at the effector cell level but not at the target cell level, although CD18 was **detectable** on the surface of monocyte targets by FACS anal. and immunopptn. Furthermore, specific binding of LAK cells to all targets tested was not affected by the presence of anti-CD18, indicating that lysis of target cells was blocked at a post-binding event. Finally, of the 3 alpha chains assocd. with CD18, only antibodies to LFA-1 (CD11a) partially blocked binding of LAK cells to monocytes and **tumor** cells. It is possible, then, that both CD11a and CD18 may work in concert to effect the lysis of target cells by LAK cells.

L17 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:532382 HCAPLUS
DOCUMENT NUMBER: 111:132382
TITLE: CD11/CD18-independent neutrophil adherence to inducible endothelial-leucocyte adhesion molecules (E-LAM) in vitro
AUTHOR(S): Dobrina, A.; Schwartz, B. R.; Carlos, T. M.; Ochs, H. D.; Beatty, P. G.; Harlan, J. M.
CORPORATE SOURCE: Inst. Gen. Pathol., Univ. Trieste, Trieste, 34127, Italy
SOURCE: Immunology (1989), 67(4), 502-8
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanisms involved in neutrophil adherence to cultured human umbilical vein endothelial cells (HEC) induced by direct stimulation of the neutrophils by phorbol myristate acetate (PMA), formylmethionyl-leucyl-phenylalanine (FMLP), or the calcium ionophore A23187 (neutrophil-dependent adherence), or by pretreatment of HEC with interleukin-1 (IL-1), **tumor** necrosis factor (TNF) or lipopolysaccharide (LPS) (endothelial-dependent adherence) were examd. Two distinct mechanisms for neutrophil adherence to HEC were demonstrated by performing adherence assays: (i) at 37.degree. vs. 4.degree.; (ii) in the presence of Ca2+ only vs. Mg2+ only; and (iii) in the presence or absence of monoclonal antibodies (mAb) to the **CD11**/CD18 adhesion complex of neutrophils. A **CD11**/CD18-dependent mechanism was **identified** that was active in the presence of Mg2+ only but not of Ca2+ only, and at 37.degree. but not at 4.degree.. A **CD11**

/CD18-independent mechanism was active at 4.degree. and at 37.degree., and in the presence of Ca2+ only and of Mg2+ only. Neutrophil-dependent adherence induced by FMLP or PMA occurred solely via the **CD11** /CD18-dependent mechanism, whereas endothelial-dependent adherence induced by a 4-h pretreatment with IL-1, TNF, or LPS involved both **CD11** /CD18-dependent and/independent mechanisms. **CD11**/CD18-deficient neutrophils isolated from a patent with leukocyte adherence deficiency (LAD) maintained the ability to adhere to LPS-pretreated HEC in the presence of Ca2+ only, indicating that this mechanism of adherence involves a receptor on the neutrophil distinct from **CD11**/CD18. The disappearance of the **CD11**/CD18-independent, but not of the dependent mechanism of adherence, HEC treated with TNF for 24 h suggests that the two mechanisms of neutrophil adherence also involve distinct inducible endothelial-leukocyte adhesion mols. (E-LAM).

L17 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:92844 HCAPLUS
DOCUMENT NUMBER: 108:92844
TITLE: Lysis of human monocytes by lymphokine-activated killer cells
AUTHOR(S): Djeu, Julie Y.; Blanchard, D. Kay
CORPORATE SOURCE: Coll. Med., Univ. South Florida, Tampa, FL, 33612, USA
SOURCE: Cell. Immunol. (1988), 111(1), 55-65
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human peripheral blood leukocytes (PBL), stimulated in vitro with recombinant human interleukin 2 (IL-2) for 2-7 days, lysed autologous and allogeneic monocytes in a 4-h 51Cr-release assay. The lymphokine-activated killer (LAK) cells against monocytic cells were selective in that polymorphonuclear leukocytes (PMN) and nonadherent PBLs were not lysed by these cells. Monocytes which had been cultured for 2-7 days served as better targets than uncultured cells. Also, kinetic studies demonstrated parallel activation of cytolytic activity against monocyte targets and FMEX, a natural killer cell-insensitive human **melanoma** target. Sepn. of PBLs by discontinuous d. centrifugation **identified** the effector population in the fractions enriched for large granular lymphocytes (LGL). Precursor cells expressed CD2, **CD11**, and some CD16 markers, but not CD3, CD4, CD8, CD15, Leu M3, or Leu 7. The effector population after IL-2 activation retained the phenotype of the precursor cell. Thus, IL-2 can generate LAK cells against monocytic cells, and this cytolytic activity, esp. against autologous monocytes, must be taken into account when IL-2 or LAK cells are used for immunomodulation in **cancer** patients.

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=> s e1-e2
             1 170560-45-9/BI
               (170560-45-9/RN)
             1 185238-80-6/BI
               (185238-80-6/RN)
L18          2 (170560-45-9/BI OR 185238-80-6/BI)

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L18  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   185238-80-6  REGISTRY
CN   DNA (human clone 6G2 gene Cdx1 protein cDNA plus flanks) (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   DNA (human clone 6G2 homeobox gene Cdx1 protein cDNA plus flanks)
CN   GenBank U51095
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
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CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

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REFERENCE 1: 126:208069

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L18 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN **170560-45-9** REGISTRY
CN Protein (human small intestine clone pCDX15 gene CDX1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank U51095-derived protein GI 1777772
CN Protein (human clone 6G2 gene Cdx1)
CN Protein (human clone 6G2 homoeobox gene Cdx1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

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2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:208069

REFERENCE 2: 123:331413